SULFANILAMIDE AND SULFAPYRIDIN IN THE TREATMENT OF VARIOUS INFECTIONS*

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RESULTS OF TREATMENT OF PNEUMONIA WITH SULFAPYRIDIN

From the results that have been published concerning the effect of sulfapyridin in the treatment of pneumonia in man, an attempt has been made to establish two points: (1) that fatality rates are reduced following the use of the drug, and (2) that the duration of the disease has been shortened. For example, in a series of 100 cases reported by Flippin, Lockwood, Pepper, and Schwartz,[19] a fatality rate of 4 per cent is recorded. If the three fatal cases, which were excluded because they were inadequately treated, are included, the fatality rate in the 103 observed cases is 6.7 per cent. Of these cases, *only eight showed bacteremia.* Other series of cases report fatality rates varying between 1.7 and 10 per cent. Unfortunately, many of the reports do not reveal the type of pneumococcus or the frequency of bacteremia, and the fatality rate in the control series is often stated to be between 1.7 and 22 per cent. One cannot decide, therefore, on a basis of the cases reported so far, how much one can influence the course of pneumococcic pneumonia with sulfapyridin alone in a statistically significant group with bacteremia and an expected high death rate.

The results of Finland and his associates[20] in our clinic, which were reported at the recent meeting of the American College of Physicians, are significant, since they include the results of the use of serum and sulfapyridin, alone and in combination during the same period, and information concerning age distribution and the incidence of bacteremia is available for all three groups. They found that the fatality rate in 167 cases which were treated with specific serum was 13 per cent. The incidence of bacteremia in this group was 29 per cent and, as usual, it was somewhat higher in the older-age groups. Of the ninety-five patients treated with sulfapyridin, the fatality rate was 15 per cent. However, the incidence of bacteremia in this group was only 17 per cent and, for patients over 60 years of age, only 14 per cent. This indicates quite definitely that the infection in this group was of a milder nature than the group that was treated with serum alone. The 15 per cent fatality rate in this group probably indicates a reduction in the expected fatality rate, but more cases are needed before one can be certain.

In a third group of eighty cases which were treated with both sulfapyridin and specific serum, the fatality rate was 22 per cent. This group contained a greater number of older patients and the incidence of bacteremia was 50 per cent, which is about twice that in the patients treated with serum alone and about three times that with sulfapyridin alone. From all previous experience, it would be expected that the fatality rate in such a group of patients would be considerably greater. Eighty-one per cent of the patients were over 40 years of age and 34 per cent were over 60 years of age. Among the twenty-seven patients over 60, sixteen or 59 per cent had bacteremia. From past experience in similar cases not treated by specific measures, the average fatality rate in this age group with bacteremia is between 75 and 90 per cent; with specific serum treatment it is about 50 per cent.

These observations would seem to indicate that the most effective way to use sulfapyridin is in combination with specific serum. They also suggest that sulfapyridin alone may reduce the fatality rate, especially in the milder cases in which the incidence of bacteremia is low.

The reports of Barnett, Hartmann, Perley, and Ruhoff,[21] and McKhann,[22] in the treatment of pneumococcic infections in infants and children with sulfapyridin, indicate that the drug frequently causes a definite improvement in the course of the disease within twenty-four to thirty-six hours after starting treatment.

Dosage.—In administering sulfapyridin, it is well to remember that the drug is quite insoluble and may be absorbed irregularly and slowly from the gastrointestinal tract, so that it is necessary to do quantitative examinations in the blood at frequent intervals. It is desirable to obtain a concentration in the blood of at least 5 to 7 milligrams of free sulfapyridin per 100 cubic centimeters whenever possible, and to attempt to keep this level constant until clinical improvement is definite, and then to continue it for at least three to five days. Since the sulfapyridin precipitates out of solution when the concentration is below 30 milligrams per cent, it is highly desirable to keep the fluid output up to at least 2,500 to 3,000 cubic centimeters a day.

The plan for dosage that we have used is to give 5 grams during the first 24-hour period, and then 4 grams a day until clinical improvement occurs. We have generally continued the drug, when it is given alone, for three or four days after the temperature is normal, the pulse rate has been reduced, and the signs in the lung show no evidence of spreading. Very often, one finds that the fever disappears within twenty-four and thirty-six hours, but the pulse rate continues to be elevated, and the patients still feel and look ill. This is in striking contrast to the appearance of the patient who makes a prompt recovery following specific serum treatment, since, when the temperature falls, the patient feels and looks well.

When sulfapyridin is given together with serum and the results are satisfactory, it is often possible to discontinue the drug within thirty-six hours after it is started, since many of the patients are greatly improved within this time.

Side Effects of Sulfapyridin.—A most troublesome side-effect is the anorexia, nausea, and vomiting* which occur in most of the patients. This symptom is one that may necessitate discontinuing the drug. If it occurs and the drug is not discontinued, it is imperative that the fluid intake be maintained by intravenous injection, since we have seen oliguria and nitrogen retention follow the vomiting attacks in these patients. Another point worth noting is the fact that, when vomiting occurs, very little of the drug may be absorbed, so that frequent determinations of sulfapyridin in the blood are necessary.

The other side-effects from this drug are the same as those following sulfanilamide, such as agranulocytosis, hemolytic anemia, and toxic hepatitis; and perhaps, in addition, renal damage.

All of these features must be looked for constantly in every patient receiving sulfapyridin.

SUMMARY

In summing up the results of sulfapyridin treatment of pneumococcic pneumonias, the following tentative statements would seem justifiable:

Sulfapyridin has a striking effect on the course of pneumococcic infections in infants and children at an age period when both the fatality rate and the incidence of bacteremia are low. In adults, the best results seem to be obtained when sulfapyridin is used along with specific serum. This has been brought out by Finland, Spring, and Lowell[20] in a

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* The discussion appearing in this section of CALIFORNIA AND WESTERN MEDICINE is an appendix to the article by Doctor Keefer, also printed in this issue. (See on page 81, and also the footnote on page 84.)

19. Flippin, H. F., Lockwood, J. S., Pepper, D. S., and Schwartz, L.: The Treatment of Pneumococcic Pneumonia with Sulfapyridin—A Progress Report on Observations in One Hundred Cases, J. A. M. A., 112:529, 1939.

20. Finland, M., Spring, W. C., and Lowell, F. C.: Specific Serotherapy and Chemotherapy of the Pneumococcic Pneumonias, Ann. Int. Med., 12:1816, 1939.

21. Barnett, H. L., Hartmann, A. F., Perley, A. M., and Ruhoff, M. B.: The Treatment of Pneumococcic Infections in Infants and Children with Sulfapyridin, J. A. M. A., 112:518, 1939.

22. McKhann, C. F.: Personal communication.

* Inasmuch as the vomiting is due to the central action of the drug, we have not found any way of preventing it.